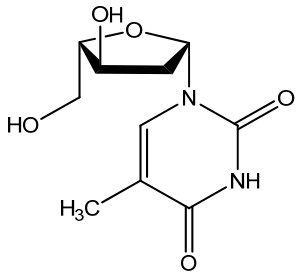
Telbivudine PK Fact Sheet

Details

Generic Name	Telbivudine
Trade Name	Sebivo®, Tyzeka®
Class	Synthetic thymidine nucleoside analogue with antiviral activity against HBV DNA polymerase
Molecular Weight	242.23
Structure	

Summary of Key Pharmacokinetic Parameters

Telbivudine is phosphorylated by cellular kinases to the active triphosphate, which has an intracellular half-life of 14 hours.

Linearity/non-linearity	Telbivudine pharmacokinetics are dose proportional over the range of 25 to 1800 mg.
Steady state	Achieved after 5-7 days of once-daily administration with an approximate 1.5-fold accumulation in systemic exposure, suggesting an effective accumulation half-life of ~15 hours.
Plasma half life	Terminal elimination half life 41.8 ± 11.8 h
Cmax	3.2 ± 1.1 µg/ml (600 mg single dose, healthy subjects). Inter-subject variability (CV%) ~30%.
Cmin	0.2-0.3 µg/ml
AUC	28.0 ± 8.5 µg.h/ml (600 mg single dose, healthy subjects). Inter-subject variability (CV%) ~30%.
Bioavailability	52% (15 mg IV and 200 mg oral dose via a 2-way crossover design)[1]
Absorption	Absorption and exposure were unaffected when a single 600 mg dose was administered with food. Telbivudine can be taken with or without food.
Protein Binding	3.3% in vitro
Volume of Distribution	Apparent volume of distribution is in excess of total body water, suggesting wide distribution into tissues. 750.0 ± 365.7 L (600 mg single dose, fasted); 668.1 ± 304.6 L (600 mg single dose, fed)[2]
CSF:Plasma ratio	Data not available
Semen:Plasma ratio	Data not available
Renal Clearance	Primary route. Renal clearance is similar to glomerular filtration rate, suggesting passive filtration is the main mechanism of excretion. Approximately 42% of a 600 mg single dose is recovered in the urine over 7 days.
Renal Impairment	The manufacturer recommends dose adjustment with creatinine clearance <50 ml/min, including those with end-stage renal disease on haemodialysis. Haemodialysis (up to 4 h) reduces systemic telbivudine exposure by approximately 23%. Telbivudine should be administered after haemodialysis. Close clinical monitoring is recommended.
Hepatic Impairment	There is no change in telbivudine pharmacokinetics in hepatic impairment compared to unimpaired subjects. No dose adjustment is necessary in hepatic impairment.

Metabolism and Distribution

Metabolised by	No metabolites of telbivudine were detected following administration of ^{14}C-telbivudine in humans. Not a substrate for CYP450
Inducer of	Not an inducer of CYP450
Inhibitor of	Not an inhibitor of CYP450
Transported by	Data not available

References

Unless otherwise stated (see below), information is from:
Sebivo® Summary of Product Characteristics, Novartis Europharm Limited.
Tyzeka® US Prescribing Information, Novartis Pharmaceuticals.

1. Zhou X, Fielman Constance B, Kleber K et al. Absolute oral bioavailability and bioequivalence of telbivudine in healthy subjects. *Clin Pharm Ther*, 2008; **83: (suppl 1)** S77, PIII-06.
2. Zhou XJ, Lloyd DM, Chao GC, Brown NA. Absence of food effect on the pharmacokinetics of telbivudine following oral administration in healthy subjects. *J Clin Pharmacol,* 2006; **46(3)**: 275-81.